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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,442	01/19/2001	Jean-Christophe Francis Audonnet	454313-3154.2	8693

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EXAMINER
ANGELL, JON E

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,442	AUDONNET ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *2,3,6-15 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/760,574* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1 3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Action is in response to the communication filed on 12/18/02, as Paper No. 13. Claims 1-20 are pending in the application and are addressed herein.

Election/Restrictions

2. Applicant's election with traverse of Group I (claims 1-19) and election of the species BRSV in Paper No. 13 is acknowledged. The traversal is on the ground(s) that 1) the inventions of Group I and Group II could be searched together without serious burden 2) it is unlikely that the method can be used with a different product or that the product could be used in a different method; 3) that the product could be made by a materially different process; 4) there are sufficiently few species, therefore it would not be a burden to search all of the claimed species. This is not found persuasive because 1) the inventions are patentably distinct and 2) searching the additional group (and species) would be a serious burden on the examiner. With respect to applicants arguments regarding search burden, it is respectfully pointed out that the searches required for the two groups are not co-extensive because different searches are required for each group. For instance, Group II is drawn to a kit comprising a composition in containers with instructions on how to use the composition. Group I is drawn to a method of using the composition. Although the searches do overlap, the searches require searching different classifications, a prima facie indication of a serious search burden. Furthermore, the search for Group II would require searching for not only the composition, but also for the composition in containers and instructions on how to use the kit. Therefore, the searches are different, and searching the additional group would be a serious burden. Regarding applicants arguments that

it is unlikely that the method can be used with a different product or that the product could be used in a different method and that the product could be made by a materially different process, it is respectfully pointed out that the inventions can be shown to be distinct if ***either or both*** of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). The previous Office Action set forth the reasons why the product could be used in a materially different processes, regardless of how "likely" it is that the product would be used for that process. With regard to Applicants arguments regarding the species election, it is respectfully pointed out that the claims encompass seven different species. The search required for each species is unique because it requires searching for each individual species (i.e. BHV, BRSV, BVDV, bPI-3, PRV, PRRSV, and SIV) in relation to a vaccine/immunological method. Therefore a serious burden does exist for searching all of the species. It is also respectfully pointed out that the burden on the applicants and the inconvenience to the public are not considered when evaluating the claims for restriction and species election.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 2, 3, 6-15 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species or invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

4. Claims 1, 4, 5 and 16-19 as they are drawn to the elected species (BRSV) are examined herein.

Specification

It is noted that a substitute specification has been submitted (Paper No. 7, 8/8/01). However, the substitute specification has not been entered because although a clean version of the substitute specification has been submitted, it is also required that that a marked up version of the specification also be submitted in addition to the clean version. See CFR § 1.125(b) which indicates,

> A substitute specification, excluding the claims, may be filed at any point up to payment of the issue fee if it is accompanied by:
> (1) A statement that the substitute specification includes no new matter; and
> (2) A marked up version of the substitute specification showing all the changes (including the matter being added to and the matter being deleted from) to the specification of record. Numbering the paragraphs of the specification of record is not considered a change that must be shown pursuant to this paragraph.

Therefore, the substitute specification has not been entered and the originally filed specification was examined.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1, 4, 5 and 16-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 210 and 211 of copending Application No. 09/760,574. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to method of inducing an immunological response against BRSV in a bovine comprising administering to the bovine the same compositions.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 4, 5, and 16-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is noted that claims 1 and 5 contain a lot of non-limiting language (such as "and/or", "optionally" and "preferably") which makes the claims confusing. It is noted that the recitation of this kind of language does not limit the claims, but does render the claims indefinite because it makes it impossible to accurately interpret the claims. For instance, claim 1 recites,

> "(a) A DNA vaccine or... wherein the DNA vaccine or... comprises a plasmid and a cationic lipid... this lipid being preferably DMRIE, and **optionally**, DOPE **and/or** GM-

CSF protein of the bovine or porcine **or** a plasmid or expression vector which expresses the GM-CSF; **and also optionally**, the nucleic acid encoding the immunogen is the sequence of a gene from which the part encoding the transmembrane domain has been deleted **and/or** the plasmid containing the nucleotide sequence encoding the immunogen also contains a stabilizing intron, preferably... and (b)... wherein (a) and (b) are administered **together in a combination or sequentially**, and sequentially can include a prime-boost administration."

Here, because or the use of the "and/or" language it is unclear if the composition can minimally comprise as element (a) of the claim:

1) a plasmid and a cationic lipid (such as DMRIE or DOPE) only; or

2) a GM-CSF protein only; or

3) a plasmid/vector which expresses the GM-CSF only.

Alternatively, the claim could be interpreted as requiring the following minimal elements:

4) a plasmid and a cationic lipid and either a GM-CSF protein or a plasmid/vector expressing GM-CSF; or

5) a plasmid and lipid and DOPE and GM-CSF protein.

Furthermore, regarding part (b) of the claim the phrase "can be administered together in a combination or sequentially" renders the claim indefinite because it appears that (a) and (b) can be administered together sequentially, and it is unclear how two things can be administered in combination sequentially.

Claims 4, 5, and 16-19 depend on claim 1 and are rejected for the same reasons.

Regarding claim 5, the phrase "(a) comprises the sequence of the BRSV F or G gene optimized..." renders the claim indefinite because it is unclear if the claim encompasses a wild-

type BRSV F gene or an optimized BRSV F gene. Furthermore, use of the "and/or" language (p. 83, line 35) does not limit the claim.

Furthermore, claim 5 recited the phrase, ""(a) comprises the sequence of the BRSV F or G gene **optimized by substitution, by a signal sequence,** in particular that of the tPA of human origin, **of the signal sequence of the F or G protein of BRSV, and/or by the deletion of the DNA fragment encoding the transmembrane domain of G or G**". This phrase is totally confusing and can not be accurately interpreted. Amendment of the claim is required.

Considering the vague language of the claims (because of all of the "and/or" language), it is extremely hard to interpret the claim. However, the Examiner will make the best effort possible to completely search the claims. For examination purposes, claim 1 is interpreted as being only limited to:

An immunological composition comprising

A

1) a plasmid containing a nucleotide sequence encoding an immunogen wherein the immunogen is expressed in vivo and

2) a cationic lipid (as set forth in claim 1, lines 9-16 (such as DMRIE)

and

B

An immunological composition against a bovine/porcine pathogen (i.e. an adjuvant),

Wherein **A** and **B** are administered together in combination or separately (i.e. sequentially).

For examination purposes, and in light of the confusing language, claim 5 is interpreted as only being limited to:

The method of claim 4 wherein the immunological composition according to A comprises the sequence of BRSV-F

(Note: it appears that claims 1 and 5 could be made more definite by separating the elements into new dependent or independent claims).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 4, 5, 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al. (Journ. General Virology 1997, 78:3195-3206) in view of Harris et al. (US Patent 5,719,131; 1998) and further in view of Bonnem et al. (WO 94/01133, listed in IDS as reference AJ) and Baker et al. (US Patent 5,106,733; 1992).

Taylor teaches a DNA vaccine against a bovine pathogen (specifically, BRSV) comprising a nucleic acid encoding an immunogen of a pathogen of the animal species considered (here, the F and G proteins of BRSV), under conditions allowing the in vivo expression of this sequence (see p. 3195, abstract; p. 3199, Figure 2; and p. 3200, under "Effect of vaccination on BRSV infection").

Taylor does not teach that: 2) the vaccine comprises a cationic lipid containing a quaternary ammonium salt (such as DMRIE and DOPE); 2) the vaccine comprises a GM-CSF protein of the animal species considered or a plasmid encoding said GM-CSF protein.

Harris teaches a cationic amphiphile comprised of DMRIE and DOPE, which can be complexed to therapeutic molecules and used to facilitate the transport of the therapeutic molecules (such as plasmid DNA) into target cells in a subject (see abstract; and column 40, lines 45-52). Harris teaches "the complex structure, behavior and environment presented by an intact tissue that is targeted for intracellular delivery of biologically active molecules often interfere substantially with such delivery..." Administration of the amphiphile facilitates the transport of the therapeutic molecules into cells.

Bonnem teaches that GM-CSF can be used as a vaccine adjuvant for enhancing the immune response of a mammal to a vaccine comprising administering to such a mammal an effective amount of GM-CSF in conjunction with a vaccine (see abstract). Bonnem indicates

that "in conjunction" refers to administration of GM-CSF concurrently, before or following administration of a vaccine (see p. 3, lines 31-32). Bonnem does not teach that the GM-CSF administered is bovine GM-CSF.

Baker teaches a cDNA sequence encoding bovine GM-CSF and methods of expressing bovine GM-CSF in a cell using an expression vector (see Figure 1; column 1, lines 55-68; and column 6, line 13 through column 8, line 25).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to combine the teachings of Taylor, Harris, Bonnem and Baker to create a method of obtaining an immunogenic response comprising administering to a bovine an immunological composition comprising a nucleic acid sequence encoding an the BRSV F gene (an immunogen of the BRSV pathogen) and a cationic lipid (such as DMRIE:DOPE) and also bovine GM-CSF. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to administer the bovine GM-CSF either together with the DMRIE:DOPE BRSV vaccine composition (in combination) or separately (i.e. sequentially), with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to combine the teachings to create the claimed method in order to create increase the efficacy of the BRSV vaccine by making modifications that were known in the art (as mentioned above, see Harris) such as complexing DMRIE:DOPE to the therapeutic nucleic acid and expressing the BRSV immunogens in order to facilitate the delivery of the plasmids into cells where the immunogen

could be expressed (e.g., BRSV F gene, see Taylor) and further comprising bovine GM-CSF to enhance the host's immune response to the BRSV vaccine (see Bonnem and Baker, above). It would have been obvious to add a GM-CSF to the vaccine because Bonnem teaches that GM-CSF enhances the immune response to vaccines (see above). It also would have been obvious to use bovine GM-CSF (taught by Baker) because Taylor teaches that the vaccine is intended for bovines. Furthermore, it would have been obvious to one of skill in the art to administer the vaccine:lipid complex (A) and the bovine GM-CSF (B) in any order (in combination or sequentially) because Bonnem teaches effective administration of the GM-CSF and the vaccine complex can be concurrently with, or sequentially (either before or following) to administration of the vaccine complex.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVE T. NGUYEN
PRIMARY EXAMINER

J. Eric Angell
March 9, 2003